Catlab Informa

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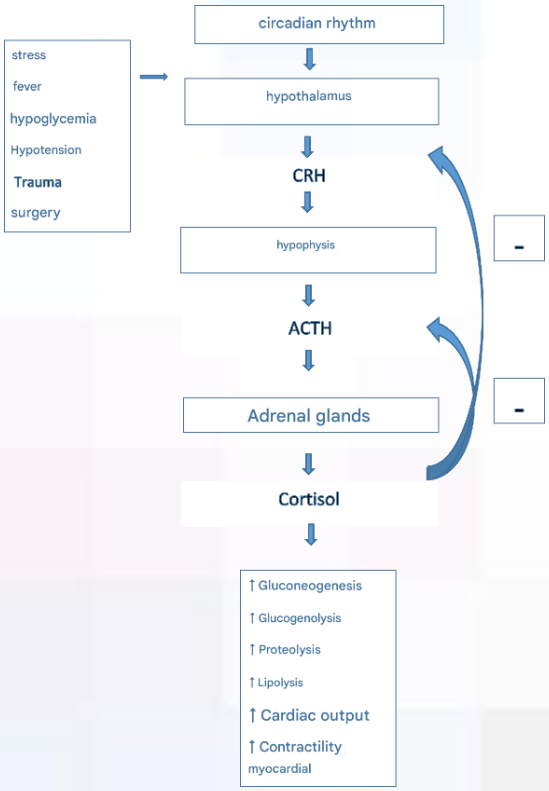
How much do you know about cortisol in saliva?

Introduction

Cortisol is a glucocorticoid secreted by the adrenal cortex in response to the action of adrenocorticotropic hormone (ACTH). It has anti-inflammatory activity, contributes in the regulation of blood pressure and stimulates the synthesis of carbohydrates from proteins. Its excretion has a circadian rhythm with a peak at 8 am and decreasing during the day.

The regulation of cortisol secretion is carried out through the hypothalamic-pituitary axis. When cortisol concentration in the blood decreases, the hypothalamus releases corticotropin-releasing hormone (CRH), which acts directly on the pituitary gland to induce the production of corticotropin (ACTH). ACTH stimulates the adrenal glands to produce and release cortisol. There is a negative feedback loop of cortisol at the hypothalamus and pituitary levels. In order to ensure proper cortisol production, it is essential that the hypothalamus, pituitary and adrenal glands function properly (Figure 1) .

Figure 1 Diagram of the regulation of cortisol secretion.



Measuring cortisol in the blood is useful for diagnosing diseases related to the adrenal cortex. Its concentration is high in patients with Cushing's syndrome and low in patients suffering from Addison's disease. One physiological cause of increased cortisol is stress.

90% of cortisol circulates bound to plasma proteins (albumin and glucocorticoid-binding globulin) and the remainder, which is the biologically active form, circulates free. Cortisol not bound to proteins diffuses freely in saliva and, therefore, its measurement more accurately reflects the concentration of free cortisol in the blood. The concentration of cortisol in saliva is not affected by salivary flow or by the enzymes found in saliva. The patient can obtain the sample at home, which reduces stress.

Applications

There are multiple applications of the determination of hormones in saliva, among which cortisol in saliva stands out. Since 2008, the European Society of Endocrinology and the American Association of Clinical Chemistry have recommended the use of cortisol in saliva at 11 pm as a screening technique for Cushing's syndrome.

Currently, the established applications for cortisol in saliva are:

- **Circadian rhythm alterations and hypercortisolism**.
    - Analysis of the circadian rhythm in hypercortisolism and adjustment of medical treatment to improve circadian cortisol (cortisol rhythm 6-8 points).
    - De novo diagnosis, relapse or recurrence of neoplastic hypercortisolism: Cushing's syndrome (nocturnal salivary cortisol).
    - Evaluation of the cyclicity of secretion in cyclic Cushing's syndrome (nocturnal salivary cortisol).
    - Evaluation of the circadian rhythm in different situations (cortisol curve).
- **Hypocortisolism**.
    - Study of the cortisol response after ACTH stimulation for the diagnosis of adrenal insufficiency. This application is not as well established, but could be very useful in pediatric patients due to ease of sample collection.

In the applications mentioned above, for correct interpretation, the different sources of variability in cortisol concentration must be taken into account:

- *Biological variability* due to non-modifiable factors (diurnal profile of salivary cortisol, inter and intraindividual variation, seasonal variation, effects of the patient's age and sex).
- *Biological variability* due to modifiable factors (lifestyle, diet, medication, tobacco, alcohol, physical activity).
- *Methodological variability.* Due to both the preanalytical processes (related to sample collection and storage) and the analytical ones (method used).
    - Regarding preanalytical phase, it is essential that the patient follows the collection instructions established by the laboratory (the type of collection tube is important, to avoid interference). Samples in which the presence of blood is observed should be discarded (the concentration in blood is higher than in saliva and could interfere).

Analytical methods

Immunoassays have been the method of choice for most laboratories for the determination of cortisol in serum or plasma, despite the limitations of these methods. These limitations include the low specificity of the associated antibodies and the need to previously separate cortisol from its carrier protein in order to analyze it. These facts and the lack of a single reference material mean that there is a great variability between the different immunoassays on the market.

Currently, LC-MS/MS methods are considered the reference methods due to their high specificity, although they are not available in all laboratories.

Advantages and disadvantages of using cortisol in saliva compared to cortisol in serum and 24-hour urine.

Advantages

- Non-invasive sample collection.
- Possibility of collecting the sample at home.
- Ease of collecting several samples during the day (circadian rhythm study).
- Possibility of sample delivery the next day.
- Fewer methodological interferences due to it being free cortisol.

Disadvantages

- Since the physiological concentration of cortisol in saliva is much lower than in serum, we are very close to the detection limit of the currently used methods. This explains the fact that more applications have been implemented in the case of hypersecretion than hyposecretion of cortisol.

Currently, Catlab participates in carrying out tests in several saliva cortisol studies to assess the stress and anxiety of patients and healthcare professionals in different situations.

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Dra. Eva Guillén Campuzano
Coordinadora Área de Bioquímica
CATLAB
Tel. 93.748.56.00 - ext. 35040 / 660676790
eguillen@catlab.cat
www.catlab.cat

Dra. Catrina Colomé Mallolas
Facultativa de Bioquímica
CATLAB
Tel. 937485600 ext. 35007/ 628192841
ccolome@catlab.cat
www.catlab.cat

Elsa Escuder Azuara
Facultativa de Bioquímica
CATLAB
Tel. 937485600 ext. 35007/ 650850749
eescuder@catlab.cat
www.catlab.cat

Amaia Fernández Uriarte
Facultativa de Bioquímica
CATLAB
Tel. 937485600 ext. 35007/ 681342975
afuriarte@catlab.cat
www.catlab.cat

Gemma Ferrer Orihuel
Facultativa de Bioquímica
CATLAB
Tel. 937485600 ext. 35007/ 628599821
gferrer@catlab.cat
www.catlab.cat